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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/270,983	03/17/1999	BRUCE A. HAY	CIT1130-1	3362

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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 09/09/2003

38

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/270,983	HAY ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,57 and 58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,8, 57 and 58* is/are rejected.

7)☐ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/20/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/27/2003 has been entered.

Applicants amendment of the title and claims 1 and 58, Paper No. 29, 7/8/2002, is acknowledged.

Claims 1-8, 57 and 58 are at issue and are present for examination.

Applicants' arguments filed on 7/8/2003, Paper No. 29, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claim 6 is objected to because of the following informalities: Claims 5, 6 and 8 are objected to because they depend from rejected claims 3 and 1. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicants amendment of the claims and traversal of the earlier 112 first paragraph rejections is acknowledged, as the previous rejections were based on the lack of written description and lack of an enabling disclosure for the claimed fusion protein(s) comprising a repressor polypeptide that represses the activity of the reporter polypeptide by conferring specific localization in a cell such that the reporter polypeptide has reduced activity, wherein said reporter polypeptide is linked to the linker polypeptide, and wherein cleavage of said linker polypeptide at said protease cleavage site increases the activity of said reporter. Applicants have amended the claims such that the claims are no longer directed to a fusion protein that "wherein cleavage of said linker polypeptide at said protease cleavage site increases the activity of said reporter". The rejections below under 112 first paragraph are based on a lack of description and lack of enabling disclosure for a fusion protein comprising a repressor polypeptide that represses the activity of the reporter polypeptide by conferring specific localization in a cell such that the reporter polypeptide has reduced activity, wherein said reporter is any enzyme.

Claims 1-4, 7 and 58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4, 7 and 58 are directed to all possible fusion proteins comprising a repressor polypeptide that represses the activity of the reporter polypeptide by conferring specific localization in a cell such that the reporter polypeptide has reduced activity, wherein said reporter polypeptide is linked to the linker polypeptide, and wherein upon cleavage of said linker polypeptide at said protease cleavage site an increase in the activity of said reporter polypeptide can be detected, wherein said reporter polypeptide can be any enzyme. Specifically applicants claims are directed to those fusion proteins, wherein said reporter can be any enzyme and said repressor must repress said "any enzyme reporter" by conferring specific localization in a cell.

Applicants have failed to describe even a single species of those fusion proteins encompassed by the claimed fusion proteins such that the reporter polypeptide comprises a enzyme which is repressed by conferring specific localization in a cell.

Thus, the specification fails to describe any representative species and/or characteristics of those fusion proteins comprising a repressor polypeptide that represses the activity of the reporter polypeptide by conferring specific localization in a cell such that the reporter polypeptide has reduced activity, wherein said reporter polypeptide is linked to the linker polypeptide, and wherein said reporter is an enzyme. Applicants comments in response to the previous 112 first paragraph rejection are acknowledged. Specifically applicants comments that the specification discloses several examples of enzyme reporter polypeptides (page 10, lines 6-15) and repressor

polypeptides that direct specific localization in a cell (page 13, line 15 to page 15, line 4). It is pointed out to applicants that the referred to disclosure of enzyme reporter polypeptides and repressor polypeptides that direct specific localization in a cell does not adequately support those fusion proteins comprising an enzyme which must be repressed specific localization in a cell. As no predictability of structure is apparent for the claimed genus and given the lack of disclosed species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-4, 7 and 58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for those fusion proteins comprising a reporter polypeptide and a repressor polypeptide that represses the activity of the reporter polypeptide by conferring a specific localization in the cell such that the attached reporter has reduced activity, wherein said reporter polypeptide is a transcriptional activator, does not reasonably provide enablement for a fusion protein comprising a reporter polypeptide and a repressor polypeptide that represses the activity of the reporter polypeptide by conferring a specific localization in the cell such that the attached reporter has reduced activity, wherein said reporter polypeptide is a any

enzyme. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Applicants have given no guidance as to how make a fusion protein comprising a repressor polypeptide that represses the activity of the reporter polypeptide by conferring specific localization in a cell such that the reporter polypeptide has reduced activity, wherein said reporter polypeptide is linked to the linker polypeptide, and wherein upon cleavage of said linker polypeptide at said protease cleavage site an increase in the activity of said reporter polypeptide can be detected, **wherein said reporter polypeptide is an enzyme.** Specifically applicants have not given guidance as to how to make such a fusion protein, such that it comprises a reporter which is repressed by a repressor which does so through cellular localization.

Because of this lack of guidance, and the extended experimentation that would be required, it would require undue experimentation for one skilled in the art to make the claimed fusion proteins.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 3, 5, 57, 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Sakai et al. (Cell, Vol 85, pp 1037-1046, 1996)

Sakai et al. teach a H-Ras-SREP-2 fusion protein comprising a NH2-terminal segment of approximately 500 amino acids, which projects into the cytosol and comprises a transcription factor (reporter polypeptide), linked to a middle segment which comprises a helical hairpin membrane anchor (repressor polypeptide) consisting of two transmembrane helices followed by an approximate 500 amino acid in length carboxy-terminal segment. Further the taught fusion protein comprises a protease cleavage site near the first transmembrane domain, which upon cleavage releases the NH2-terminal segment which then enters the nucleus and activates transcription by binding to a 10 bp sterol regulatory element. Sakai et al. further teach that in addition to sterol-regulated proteolysis, SREBP-2 can be cleaved in a sterol-independent manner

by CPP-32 and Mch-3, two cysteine proteases that are activated during programmed cell death.

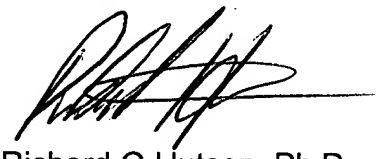
Claims 1, 3, 5, 8, 57, 58 are rejected under 35 U.S.C. 102(e) as being anticipated by Crabtree et al. (U.S. Patent No. 5,380,462).

Crabtree et al. teach a number of chimeric proteins comprising at least one ligand-binding (or "receptor") domain fused to an additional "action" domain, wherein the chimeric proteins are derived from different sources not normally found together in nature. Crabtree et al. teach that the action domain may be a transcriptional activator (See column 13, lines 42-61) or additional regulatory systems such as protein kinase or phosphatase activities. Crabtree further teach that the chimeric protein may have an intracellular targeting domain which targets the chimeric protein to the plasma membrane (See column 12, lines 29-36 and Figure 18). While Crabtree et al. do not describe the specifically taught domains as per the instant inventors, (i.e. "repressor polypeptide", "reporter polypeptide" and "linker polypeptide") the chimeric proteins taught by Crabtree et al. anticipate the instantly claimed "fusion proteins".

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh